Persistent mortality and heart failure burden of anterior ST-segment elevation myocardial infarction following primary percutaneous coronary intervention: real-world evidence from the US Medicare Data Set

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ABSTRACT

Objectives We sought to compare the temporal trends in the incidence of death and rehospitalisation for congestive heart failure (CHF) following anterior ST-elevation myocardial infarction (STEMI) in a Medicare cohort of beneficiaries treated with primary percutaneous coronary intervention (PCI) in 2005 (n=1479) with those treated in 2016 through quarter (Q) 2 of 2017 (n=22432).

Design This retrospective analysis examined outcomes using both descriptive and regression analysis to control for differences in patient clinical characteristics over time.

Primary outcome measures The primary outcomes are 1 year and 2 year rates of mortality and re-hospitalisation for CHF.

Results The 1 year mortality rate was numerically higher in the 2016 cohort at 10.3% (95% CI 9.9 to 10.7) versus 8.9% (CI 7.4 to 10.3; p=0.068). The 2 year mortality rate was significantly higher in the 2016 cohort at 14.5% (CI 13.9 to 15.1) versus 11.4% (CI 9.2 to 13.6; p<0.01). The 1 year rehospitalisation for CHF was lower in the 2016 cohort at 10.6% (CI 10.0 to 11.2) versus 16.7% (CI 14.0 to 19.4; p<0.001), but the 2 year rate was not significantly different at 19.3% (CI 17.7 to 20.9) versus 20.7% (CI 16.4 to 24.9; p=0.55). After adjustment for covariates with two models, the 1 year mortality increased by 2.3% (CI 0.8 to 3.7; p<0.01) and 4.1% (CI 2.6 to 5.6; p<0.001) in the 2016 cohort. The 2 year adjusted mortality also increased by 4.2% (CI 2.0 to 6.4; p<0.001) and 6.5% (CI 4.2 to 8.7; p<0.001) in the 2016 cohort. The risk adjusted trends for rehospitalisation for CHF were similar to the unadjusted findings.

Conclusions Despite prior improvements in STEMI outcomes in the reperfusion era related to the broad adoption of timely PCI, there is a persistent high mortality and CHF burden in Medicare beneficiaries with anterior STEMI. New strategies that address reperfusion injury and enhance myocardial salvage are needed.

INTRODUCTION

Ischaemic heart disease remains the leading cause of death worldwide. Over 15 million acute myocardial infarctions (MI) occur annually and 40% of these are ST-elevation myocardial infarction (STEMIs) requiring emergent reperfusion therapy.1 2 The more widespread availability of timely reperfusion therapy, initially with thrombolysis and subsequently with primary percutaneous coronary intervention (PCI) resulted in a steady decline in post-MI mortality in many developed countries.3 6 However, registry data suggest that there may be a plateau in these mortality improvements that was reached after national initiatives maximised access to primary PCI with stenting in developed markets.4 5 The observed improvements in clinical outcomes over time in all comers with STEMI could potentially be influenced by advancements in the PCI procedure or in secondary prevention measures in addition to the more widespread use of timely PCI.4 6 Separating the impact of PCI utilisation from the impact of these other potential advancements over time requires analysis of outcomes for comparable STEMI patients treated with primary PCI in different years. Published data on these temporal trends are limited, particularly with
follow-up beyond 1 year and in real-world primary PCI populations that include the higher risk patients often excluded from randomised trials. Several studies suggest that the incidence of congestive heart failure (CHF) post-STEMI may have also decreased in the reperfusion era. However, these data come from relatively small studies and there are conflicting reports suggesting an increased incidence of CHF in patients surviving the acute STEMI event. Further data are needed to address these crucial issues which relate to where continued efforts should be focused to mitigate the ongoing burden of STEMI. We thus sought to compare the temporal trends in the incidence of death and rehospitalisation for CHF following STEMI in Medicare beneficiaries treated with primary PCI in 2005 with those treated from 2016 to quarter (Q) 2 of 2017. Given the higher expected event rates in patients with anterior wall STEMI, the focus of this analysis is on this high-risk group.

METHODS
Medicare data were accessed under a Data Use Agreement with the Centres for Medicare and Medicaid Services. The changes in 1 year rates of mortality and rehospitalisation for CHF in patients treated for anterior STEMI in 2005 versus 2016 and Q1–Q2 of 2017 were examined using both descriptive and regression analyses. In order to allow for adequate follow-up, data were obtained from the 2005–2008 5% and the 2016–Q2 2019 100% Medicare Inpatient Limited Data Set populations. Patients discharged from an acute care hospital with a principal diagnosis of anterior STEMI were identified by ICD-9 diagnosis codes 410.00, 410.01, 410.10 and 410.11 or ICD-10 diagnosis codes I21.01, I21.02 and I21.09. Treatment with PCI with stenting was required and was identified in the 2005 data by MS-DRGs 121, 122, 124, 126, 526, 555 and 557 and in the 2016 data by MS-DRGs 246 and 247. Patients with cardiogenic shock were excluded by eliminating patients with ICD-9 diagnosis code 785.51 and ICD-10 diagnosis code R57.0. This was done to avoid the potential confounding of the results by the inclusion of more shock patients in the 2016 cohort. The 2005–2007 Medicare Inpatient Limited Data sets only report the quarter of discharge from the hospital. Therefore, the 4-quarter as well as 8-quarter rates for mortality and rehospitalisation for CHF were assessed during this time frame and are reported as 1 year and 2 year rates. The sample was divided into two cohorts based on the year of discharge from the hospital. The first cohort included cases discharged in 2005 and the second cohort included cases discharged in 2016 and in Q1–Q2 of 2017. The difference in outcomes between the 2005 and 2016 cohorts was assessed with t-tests. Regression analysis was also performed to control for differences in patient clinical characteristics over time. Medicare claims in 2005 reported only nine secondary diagnoses, whereas claims in 2016–2017 reported 24 secondary diagnoses. To ensure consistency in identifying comorbidities across the time frame, the first nine secondary diagnoses were utilised in the 2016–2017 claims. The key independent variable in the regression analyses was an indicator for 2016 cohort.

We estimated a linear regression of each outcome using the two risk adjustment strategies. In one set of regressions, propensity score matching (PSM) adjustment variables included age, sex, race/ethnicity, diabetes mellitus, hypertension, hyperlipidaemia, atrial fibrillation and antioventricular block. In the second set of regressions, we controlled for Elixhauser comorbidities in addition to age, sex and race/ethnicity. In all regressions, we controlled for the quarter of hospitalisation.

RESULTS
The baseline demographics and for the 2005 (n=1479) and 2016 (n=22432) cohorts are outlined in table 1. The 2016 cohort was younger and had fewer females and Caucasian patients compared with the 2005 cohort. The 2016 cohort had a higher Elixhauser Index with significantly more hypertension and hyperlipidaemia. In addition, diabetes was more frequent in the 2016 cohort with 1 year of follow-up. Atrioventricular block was less frequent in the 2016 cohort (table 1).

Unadjusted outcomes are presented in table 2 and figure 1 with point estimates and 95% CIs. Among Medicare beneficiaries diagnosed with anterior STEMI who are treated with PCI with stenting, the 1 year mortality rate was numerically higher in the 2016 cohort at 10.3% versus 8.9% in the 2005 cohort, p=0.07. The 2 year mortality rate was significantly higher in the 2016 cohort at 14.5% versus 11.4% in the 2005 cohort, p=0.01. One-year rehospitalisation for CHF was higher in the 2005 cohort at 16.7% versus 10.6% in the 2016 cohort, p=0.01, but the 2 year rate was not significantly different (20.7% vs 19.3%, p=0.55).

Risk-adjusted event rates are presented in table 3. After controlling for differences in clinical characteristics between 2005 and 2016 cohorts using Elixhauser co-morbidities, there are statistically significant increases in the 1 year and 2 year mortality rates in the 2016 cohort of 2.3 and 4.2 percentage points, respectively. When controlling for differences in clinical characteristics using the PSM variables, there are similar statistically significant increases in 1 year and 2 year mortality rates in the 2016 cohort of 4.1 and 6.5 percentage points. Risk-adjusted 1 year rehospitalisation rate for CHF decreased by 4.9 and 6.9 percentage points between the 2005 and 2016 cohorts with the PSM and Elixhauser risk adjustments, respectively. However, there is no significant change in the 2 year rehospitalisation rate for CHF between the 2005 and 2016 cohorts with either risk adjustment model.

Patient and public involvement statement
There was no patient or public involvement in the design, conduct or reporting of this work.
The event rates for the male and female subgroups are presented in Table 4. Of note is that the 1-year mortality rate was significantly higher for women in the 2016 cohort. In men, the 1-year mortality for the 2016 cohort was numerically higher as it was in the combined cohorts. The 2-year mortality rate was also significantly increased in females, whereas in men, it was numerically higher, but not significantly higher as it was in the combined cohorts. The findings related to rehospitalisation for CHF were similar in males and females.

DISCUSSION

This analysis of outcome trends among Medicare beneficiaries who are diagnosed with anterior STEMI and treated with PCI yielded several important findings. Over time, there was a numerically higher 1-year unadjusted mortality and a statistically significant increase in 2-year unadjusted mortality. Furthermore, the risk-adjusted 1-year and 2-year mortality rates increased significantly between the 2005 and 2016 cohorts when controlling for changes in clinical characteristics with the two different regression models. There was a significant decrease in the unadjusted and risk-adjusted 1-year rehospitalisation rates for CHF over time, but no significant change in the 2-year rehospitalisation rates for CHF in either the unadjusted or risk-adjusted analyses.

The reduction in mortality for patients with STEMI in the reperfusion era is a major accomplishment of cardiovascular medicine. However, national registries suggest that there may not have been further progress after maximising the benefit of early PCI in developed markets.3–5 The rates of mortality and rehospitalisation for CHF in the present analysis support the premise that there has been no significant improvement in the last decade for STEMI outcomes when considering patients who received timely primary PCI with stenting. There are limited prior data focusing on these event rates over time only in patients treated with primary PCI for anterior STEMI. This is particularly the case for data on all-comers including patients not enrolled in randomised

Table 1  Baseline demographics

<table>
<thead>
<tr>
<th>Patient characteristic</th>
<th>2005 cohort n=1479</th>
<th>2016 cohort n=22432</th>
<th>Difference</th>
<th>P value</th>
<th>2005 cohort n=798</th>
<th>2016 cohort n=12786</th>
<th>Difference</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>73.6±11.1</td>
<td>71.2±10.0</td>
<td>−2.4</td>
<td>&lt;0.01</td>
<td>73.4±10.8</td>
<td>71.3±9.9</td>
<td>−2.1</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Female</td>
<td>48.8%</td>
<td>34.7%</td>
<td>−14.1%</td>
<td>&lt;0.01</td>
<td>50.6%</td>
<td>35.0%</td>
<td>−15.6%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>White</td>
<td>88.6%</td>
<td>86.7%</td>
<td>−1.9%</td>
<td>0.03</td>
<td>88.2%</td>
<td>87.4%</td>
<td>−0.8%</td>
<td>0.48</td>
</tr>
<tr>
<td>Black</td>
<td>7.2%</td>
<td>6.2%</td>
<td>−1.0%</td>
<td>0.14</td>
<td>7.5%</td>
<td>5.8%</td>
<td>−1.7%</td>
<td>0.08</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1.2%</td>
<td>1.5%</td>
<td>0.3%</td>
<td>0.43</td>
<td>1.4%</td>
<td>1.4%</td>
<td>0.0%</td>
<td>0.89</td>
</tr>
<tr>
<td>Conditions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>23.9%</td>
<td>27.6%</td>
<td>3.7%</td>
<td>&lt;0.01</td>
<td>26.1%</td>
<td>27.5%</td>
<td>1.4%</td>
<td>0.37</td>
</tr>
<tr>
<td>Hypertension</td>
<td>60.8%</td>
<td>70.3%</td>
<td>9.5%</td>
<td>&lt;0.01</td>
<td>61.0%</td>
<td>69.8%</td>
<td>8.8%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Hyperlipidaemia</td>
<td>44.6%</td>
<td>58.0%</td>
<td>13.4%</td>
<td>&lt;0.01</td>
<td>43.2%</td>
<td>58.6%</td>
<td>15.4%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>13.8%</td>
<td>12.2%</td>
<td>−1.6%</td>
<td>0.08</td>
<td>13.3%</td>
<td>11.9%</td>
<td>−1.4%</td>
<td>0.25</td>
</tr>
<tr>
<td>AV block</td>
<td>5.6%</td>
<td>2.5%</td>
<td>−3.1%</td>
<td>&lt;0.01</td>
<td>6.6%</td>
<td>2.4%</td>
<td>−4.2%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Elixhauser index</td>
<td>2.54</td>
<td>2.70</td>
<td>0.16</td>
<td>&lt;0.01</td>
<td>2.53</td>
<td>2.66</td>
<td>0.13</td>
<td>0.02</td>
</tr>
</tbody>
</table>

AV block, atrioventricular block.

Table 2  Rates of mortality and rehospitalisation for CHF by year

<table>
<thead>
<tr>
<th>Outcome</th>
<th>2005 cohort mean (%)</th>
<th>2005 cohort 95% CI</th>
<th>2016 cohort mean (%)</th>
<th>2016 cohort 95% CI</th>
<th>Unadjusted difference in mean outcome (%)</th>
<th>P value</th>
<th>Unadjusted difference 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 year mortality</td>
<td>8.9</td>
<td>(7.4 to 10.3)</td>
<td>10.3</td>
<td>(9.9 to 10.7)</td>
<td>1.4</td>
<td>0.068</td>
<td>(−0.1 to 2.9)</td>
</tr>
<tr>
<td>1 year rehospitalisation for CHF</td>
<td>16.7</td>
<td>(14.0 to 19.4)</td>
<td>10.6</td>
<td>(10.0 to 11.2)</td>
<td>−6.1</td>
<td>&lt;0.001</td>
<td>(−8.8 to 3.4)</td>
</tr>
<tr>
<td>2 year mortality</td>
<td>11.4</td>
<td>(9.2 to 13.6)</td>
<td>14.5</td>
<td>(13.9 to 15.1)</td>
<td>3.1</td>
<td>0.009</td>
<td>(0.8 to 5.4)</td>
</tr>
<tr>
<td>2 year rehospitalisation for CHF</td>
<td>20.7</td>
<td>(16.4 to 24.9)</td>
<td>19.3</td>
<td>(17.7 to 20.9)</td>
<td>−1.4</td>
<td>0.547</td>
<td>(−5.9 to 3.1)</td>
</tr>
</tbody>
</table>

CHF, congestive heart failure.
A recent systematic review examining trends in PCI outcomes from 25 all-comers trials excluded STEMI patients.15

The present analysis both finds no improvement in mortality over time in the anterior STEMI population treated with timely PCI and also suggests a potential worsening. Given that these findings are demonstrated with two different risk-adjustment models, it is not likely that this is attributable to applying primary PCI to higher risk patients over time. In this regard, patients with cardiogenic shock were excluded from the present analysis to control for the potential of more frequent triage of these high-risk patients to primary PCI over time and for the variable standard of care practices particularly related to the timing and choice of device escalation. The more widespread adoption of mechanical circulatory support in recent years may well translate into improved outcomes for this high-risk subgroup of STEMI patients experiencing cardiogenic shock.16 Nonetheless, the present data suggest that there is a continued high mortality burden in Medicare beneficiaries with anterior STEMI treated with PCI in contemporary practice as evidenced by 1 year and 2 year death rates of 10.3% and 14.5% in the 2016 cohort even after excluding patients with cardiogenic shock.

The explanation is not clear for the apparent improvement over time in the 1 year rehospitalisation rates for CHF which did not persist after longer follow-up. More effective use of standard of care medications for CHF may account for these improved outcomes, but that effect would be expected to be maintained at the 2 year analysis. It should be noted that during the follow-up of the 2016 cohort, there were payment policy changes related to early rehospitalisation for CHF which may have affected hospital coding.17,18 These payment policy changes were followed by a well-documented decrease in per capita admissions for CHF in the USA after 2014.19 Whether coding issues or an increased use of outpatient treatments for worsening heart failure accounts for these findings is not settled.19 Regardless of the explanation for these findings, there is clearly a high persistent burden of CHF in Medicare beneficiaries with anterior STEMI treated with PCI based on the 1 year and 2 year rehospitalisation rates for CHF of 10.3% and 19.6%, respectively, in the 2016 cohort analysed in this study. These findings are consistent with a recent report on trends in post-MI

![Figure 1](https://example.com/figure1.png)

**Figure 1** Rates of mortality and rehospitalisation for CHF by year. Point estimates and 95% CIs. CHF, congestive heart failure.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Risk-adjusted difference* using PSM risk adjusters (%)</th>
<th>95% CI for risk-adjusted difference using PSM risk adjusters</th>
<th>P value</th>
<th>Risk-adjusted difference* using Elixhauser comorbidities (%)</th>
<th>95% CI for risk-adjusted difference using Elixhauser comorbidities</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 year mortality</td>
<td>4.1</td>
<td>(2.6 to 5.6)</td>
<td>&lt;0.001</td>
<td>2.3</td>
<td>(0.8 to 3.7)</td>
<td>0.002</td>
</tr>
<tr>
<td>1 year rehospitalisation for CHF</td>
<td>−4.9</td>
<td>(−7.6 to −2.2)</td>
<td>&lt;0.001</td>
<td>−6.9</td>
<td>(−9.6 to −4.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2 year mortality</td>
<td>6.5</td>
<td>(4.2 to 8.7)</td>
<td>&lt;0.001</td>
<td>4.2</td>
<td>(2.0 to 6.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2 year rehospitalisation for CHF</td>
<td>0.8</td>
<td>(−3.8 to 5.3)</td>
<td>0.744</td>
<td>−3.8</td>
<td>(−8.3 to 0.6)</td>
<td>0.093</td>
</tr>
</tbody>
</table>

*Increase (+) or decrease (−) for 2016 versus 2005 cohort.

CHF, congestive heart failure; PSM, propensity score matching.
readmission for CHF in Medicare beneficiaries which noted a rate of 10.4% at 1 year in a less high-risk group not limited to only anterior STEMI. These findings are also consistent with an analysis of temporal trends in Medicare beneficiaries demonstrating a significant increase in CHF incidence between 2011 and 2016 in patients with prior MI in contrast to a decreased incidence in patients with other comorbidities.

CHF affects over 6 million Americans and is the leading cause of hospitalisation in older adults. These patients have a nearly 50% 5 year mortality. The direct and indirect economic burden for CHF is over $100 billion globally and over $30 billion in the USA alone. The recently completed PARADISE-HF trial demonstrated no additional benefit of sacubitril–valsartan compared with ramipril for the prevention of heart failure post-MI and confirms the ongoing burden in a population treated predominantly with PCI for STEMI. Given the increasing prevalence of CHF in an ageing population, the US economic burden related to CHF is projected to exceed $60 billion by 2030. Ongoing efforts are clearly needed to track the burden of CHF specifically in survivors of STEMI and the impact of new reperfusion strategies on outcomes.

From 2005 to 2019, there have been advances in drug eluting stent technologies and in anticoagulant, antiplatelet and other pharmacologic therapies for acute and convalescent STEMI treatment. For example, drug eluting stents have been demonstrated to reduce rehospitalisation for restenosis in STEMI patients. This reduction in restenosis may be associated with reduced mortality 5 years after STEMI, but not at earlier time points. These devices and current pharmacologic therapies designed to optimise epicardial vessel patency do not address the reperfusion injury which may account for half of the residual infarct size after STEMI. Infarct size is strongly associated with mortality and rehospitalisation for CHF after STEMI highlighting the importance of developing and implementing effective therapies to mitigate reperfusion injury.

The lack of adjunctive therapies to primary PCI to further reduce myocardial damage post-STEMI may offer an explanation for the presently observed persistence of high mortality and CHF rehospitalisation rates. Many pharmaceutical and device strategies have attempted to reduce reperfusion injury and infarct size. Despite positive results in preclinical models, these modalities have been largely ineffective in clinical trials. Supersaturated oxygen (SSO₂) therapy is the only adjunct device or drug demonstrated in an adequately powered randomised trial to reduce infarct size in STEMI patients treated with primary PCI and stenting. A recent review details the effects of this therapy at the myocardial cell and microvascular level. SSO₂ therapy is FDA approved for intracoronary delivery after left anterior descending artery stenting for STEMI and is currently undergoing further investigation for expanded indications including in the unmet need of cardiogenic shock. Other modalities to address reperfusion injury including mechanical unloading, cooling therapies and the delivery of other novel pharmaceutical agents require further study. The broader adoption of effective adjunctive myocardial salvage therapies may offer additional benefit in reducing mortality and the incidence of CHF in STEMI populations.

The explanation for the greater increases over time in the 1 year and 2 year mortality rates for women versus men is not readily apparent. These findings could be due to additional confounders that are not accounted for. For example, prior studies suggest that the increased mortality in women with STEMI may be related to prehospital delays in care leading to more prolonged untreated ischaemia.
Limitations
The changes in the baseline demographics between the 2005 and 2016 cohorts were expected, but necessitated risk adjustment. The decrease in the proportion of female and Caucasian patients in the 2016 cohort is consistent with other reports on trends in the demographics of Medicare patients with MI. The increase in comorbidities observed in the 2016 cohort is also consistent with these prior reports. The decrease in the proportion of female patients likely accounts for the somewhat younger age of the 2016 cohort given the known gender differences in the age of onset of ischaemic heart disease. Changes in Medicare Inpatient Limited Data sets related to the number of secondary diagnoses reported over time could have affected the risk adjustment approach in ways that are not readily apparent. Nonetheless, based on both the presently reported unadjusted and risk-adjusted event rates, it is clear that mortality and 2-year rehospitalisation for CHF following primary PCI for anterior STEMI have not improved significantly in recent years.

Outcomes were determined from vital status and claims data. As noted above payment policy changes related to rehospitalisation for CHF may have influenced the coding of these events to favour an improvement in the 1-year outcomes in the 2016 cohort. Other variations in coding over time could also be at play, but mortality data based on vital status are less prone to potential error. Nonetheless, the rehospitalisation rate at 2 years indicates a persistent high event rate in the 2016 cohort.

The findings of the present study are limited to Medicare beneficiaries and further investigation is required to address outcomes in younger populations. The present analysis was undertaken in anterior STEMI patients because of the known higher event rates in this population which would maximise the ability to detect potential improvements in outcomes over time. It is unlikely that improvement in outcomes would be detected in the non-anterior STEMI population. We noted that STEMI patients with cardiogenic shock were excluded from the present analysis to avoid potential bias related to a higher proportion of these patients undergoing primary PCI over time, and confounding factors such as variability in the timing and prevalence of mechanical circulatory support for these patients. The present data cannot exclude the potential for primary PCI with mechanical circulatory support to improve outcomes in this high-risk subgroup over time.

CONCLUSION
Despite prior improvements in STEMI outcomes in the reperfusion era related to the broad adoption of timely PCI, there is a persistent high mortality and CHF burden in Medicare beneficiaries with anterior STEMI. Improvement in outcomes beyond those achievable with restoring epicardial vessel patency will require implementation of strategies that enhance myocardial salvage by addressing downstream microvascular dysfunction and reperfusion injury.

REFERENCES


